UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/897,583	06/29/2001	Thomas A. Szyperski	19226/2051 (R-5655)	1224

7590 03/11/2004

Michael L. Goldman
NIXON PEABODY LLP
Clinton Square
P.O. Box 31051
Rochester, NY 14603

EXAMINER	
GAKH, YELENA G	

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 03/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/897,583	Applicant(s) SZYPERSKI, THOMAS A.
	Examiner Yelena G. Gakh, Ph.D.	Art Unit 1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-130* is/are pending in the application.

4a) Of the above claim(s) *1-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *91-130* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *03/04/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Election of claims 91-130 with traverse filed on 12/01/03 is acknowledged. In response to the Applicant's arguments regarding restriction requirements the examiner would like to notice that the NMR experiments listed in claim 91 are not unambiguously defined through particular pulse sequences, and therefore do not define specific NMR techniques. Claim 91 does not refer to the claims of Groups V and VII. Therefore, the restriction requirements are correct and are made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 91-130 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for $^{15}N/^{13}C$-labeled proteins, does not reasonably provide enablement for unlabeled proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The pulse sequences recited in the claims require high abundance of ^{13}C and ^{15}N nuclei, which can be provided only in $^{15}N/^{13}C$-labeled proteins, see Szyperski et al. (J. Bionol. NMR, 1998, IDS): "[the protein] isotope labeling becomes mandatory when ... (ii) the structural refinement shall include heteronuclear scalar coupling constants" (page 140).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. **Claims 91-102** are rejected under 35 U.S.C. 103(a) as being unpatentable over Szyperski et al. (J. Biomol. NMR, 1998, IDS) in view of CABM Standard Data (1998).

Szyperski discloses "sequential resonance assignment of medium sized $^{15}N/^{13}C$-labeled proteins with projected 4D triple resonance NMR experiments" (Title), comprising performing 3D $\underline{H}^{\alpha/\beta}\underline{C}^{\alpha/\beta}$(CO)NHN experiment, 3D HNN<u>CAHA</u> experiment and 3D HNN<<u>CO,CA</u>> experiment for assigning corresponding chemical shifts for the protein backbone.

Szyperski does not specifically disclose using 3D HCCH-COSY and 2D <u>HBCB</u>(CGCD)HD NMR experiments for assigning aliphatic and aromatic side chain chemical shifts.

CABM Standard Data discloses automated side chain assignments based on NMR techniques 3D HCCH-COSY (paragraph 17) for aliphatic and 2D RD <u>HBCB</u>(CGCD)HD (paragraph 20) for aromatic side chains.

It would have been obvious for anyone of ordinary skill in the art to add two NMR techniques disclosed in CABM Standard Data into the strategy disclosed by Szyperski in order to perform more completed assignment of signals in NMR spectra of proteins by adding assignments for the side chains to the assignment of the backbone.

7. **Claims 103-130** are rejected under 35 U.S.C. 103(a) as being unpatentable over Szyperski in view of CABM Standard Data, as applied to claims 91-102 above, and further in view of "Protein NMR" (NMR Experiments for Proteins).

Szyperski in view of CABM Standard Data do not specifically disclose other 3D experiments recited in claims 103-130 for assigning chemical shifts of various backbone and side-chain nuclei of proteins.

"Protein NMR" reviews possible 4D, 3D and 2D experiments for assigning chemical shifts of various nuclei in backbone and side chains of proteins via different pathways, the combination of which leads to complete assignment of NMR spectra, as well as determining protein structure from corresponding NOESY experiments.

It would have been obvious for anyone of ordinary skill in the art to combine various experiments listed in "Protein NMR", or to modify them in the same way taught by Szyperski with those disclosed by Szyperski and CABM Standard Data in order to obtain completely assigned NMR spectra and to determine tertiary structure of proteins from NOE data, since these are the main goals of the cited papers.

Conclusion

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. *Accelrys* discloses various heteronuclear triple resonance spectra, e.g. 3D: HNCACB + CBCACONH, 4D: HACA(CO)NNH; *Li (Development of an Integrated Software ...", 1996)* discloses algorithms for various 3D NMR experiments; *Nietlispach et al. (JACS, 1996)* disclose "an approach to the structure determination of larger proteins using triple resonance NMR experiments in conjunction with random fractional deuteration"; *"Cell Cycle/Gene Regulation" (1998)* discloses various sequences for assigning protein signals, including HCCTOCSYCONNH (Remark 210); *Sattler (EMBO Practical Course, Sept. 12-19, 2001, publication in Prog. NMR Spectrosc., 1999)* represents a full strategy for assigning NMR spectra and structural determination of proteins; *Kanelis et al. (Life, 2001)* teach "multidimensional NMR methods for protein structure determination".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yelena G. Gakh
2/23/04